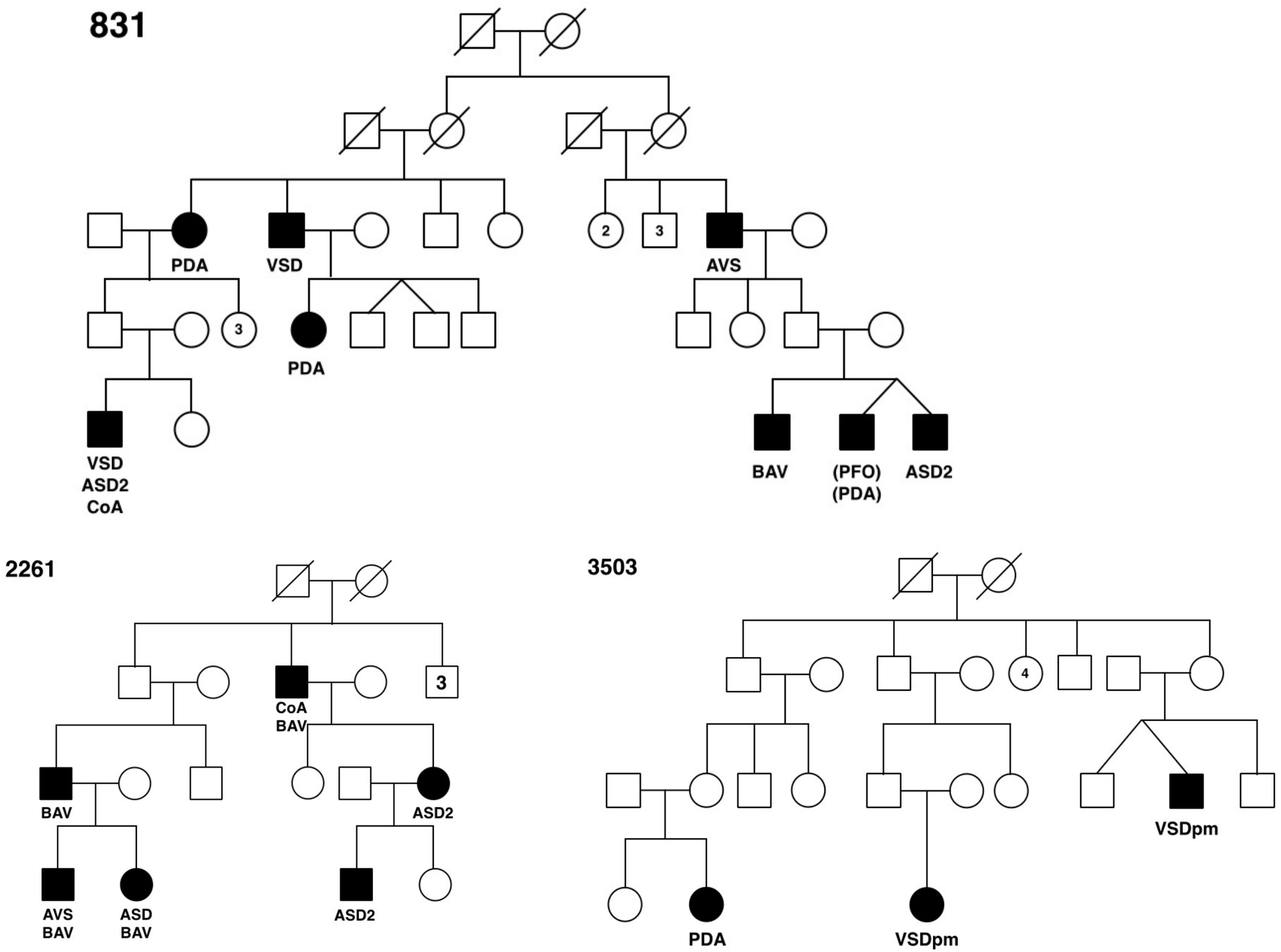
Supplementary Table I. Diagnoses of Danish probands screened for NKX2-5 mutations and their relatives

Family	Proband (M/F)	Diagnosis	Relative(s)	Relatives diagnoses
49	PS (M)	AVS	brother	TOF
53	FVH (M)	ASD2, VSDpm (PDA)	brother | father	TOF with pulmonary valve atresia | TOF
62	RBL (M)	ASD2	mother | mother's half sister	ASD2 | ASD2
223	ACW (F)	DORV Fallot type, MVS	nephew through half brother	Aortic arch atresia, PFO
231	ANP (F)	PDA	daughter | nephew	VSD | Aorta hypoplasia, PVS, VSD, PVS, ASD2 (PDA)
240	LCA (F)	ASD2	son | father	ASD | ASD
264	ADSL (F)	CoA, VSD (PDA)	nephew through sister	VSD, ASD, PDA, non-compaction right ventricle
316	CH (F)	VSD	brother	MVR
333	NK (M)	CoA	female cousin through father's sister | niece through sister	PAPVR, ASDsv | VSD
398	SSS (M)	VSD	male second cousin through father's mother's daughter	BAV, AVS
576	MHW (M)	AVS	brother | brother	BAV, Aorta dilatation | AVS, BAV
633	KJS (F)	ASD2, 1.degree AVB	Pedigree shown in Figure 1A	Diagnoses shown in Figure 1A
702	MS (M)	VSDpm	father	VSDpm
720	JC (M)	vascular ring	sister | half brother	TOF | d-TGA
732	CHK (F)	TOF	brother	TOF
770	LBN (M)	AVS	daughter	PFO
809	IMN (F)	CoA, BAV	son | grandson through affected son	PVS, BAV | AVS
831	KL (M)	AVS	pedigree shown in supplemental figure 2	diagnoses shown in pedigree supplemental figure 2
1019	DEP (M)	AVSD	sister | father	AVSD | ASD1
1117	ADVB (F)	TOF	brother	VSD
1121	MBN (F)	ASD, VSDmusc	mother's sister	PVS
1319	STA (F)	AVS	brother | mothers sister	AVS | ASD2
1560	JRK (M)	PVS	sister | sister | great-aunt through mother's mother's sister | great-cousin through mother's mother's sister's daughter	PVS | PVS | TOF | VSDpm
1710	NSH (F)	AVS, CoA, HLHS, BAV	mother | mother's sister | maternal grandmother	VSD, CoA, BAV | SV, d-TGA, VSD, MVA, PVS | ASD2
1722	SAI (M)	CoA, ASD2	niece through brother | niece through brother |	DCM | ASD2, DCM
1938	JBB (F)	TOF with PA	half sister	VSD
2198	ESN (F)	TOF with PA	brother | father	TOF with PA | TOF with PA
2261	PDJ (F)	ASD2	pedigree shown in supplemental figure 2	diagnoses shown in pedigree supplemental figure 2
2558	PLO (F)	VSD	nephew through half sister	HLHS
2893	SLWJ (F)	AVSD	son	PDA
3315	LML (F)	PLSVC, PDA	brother | mother	CoA, BAV | AVR
3500	TF (M)	TOF with PA	great-uncle through maternal grandmother	AVS
3501	CNA (M)	HLHS, PVA, ASD	male great-cousin through father's mother's sister's daughter	Ebstein, PVA
3503	PEJ (M)	VSD	pedigree shown in supplemental figure 2	diagnoses shown in pedigree supplemental figure 2
3505	RSH (M)	HLHS (PFO)	great-uncle through paternal grandfather	BAV, AVS
3506	ABR (M)	AVS, BAV	maternal grandfather	BAV, Aortic aneurysm
3508	MJ (F)	ASD	mother | maternal grandmother	SSS | ASD
3514	RS (M)	VSDpm	sister	ccAVB
3540	JM (M)	HLHS, CoA	male cousin through mother's sister | maternal grandmother	PAPVR | ASD2

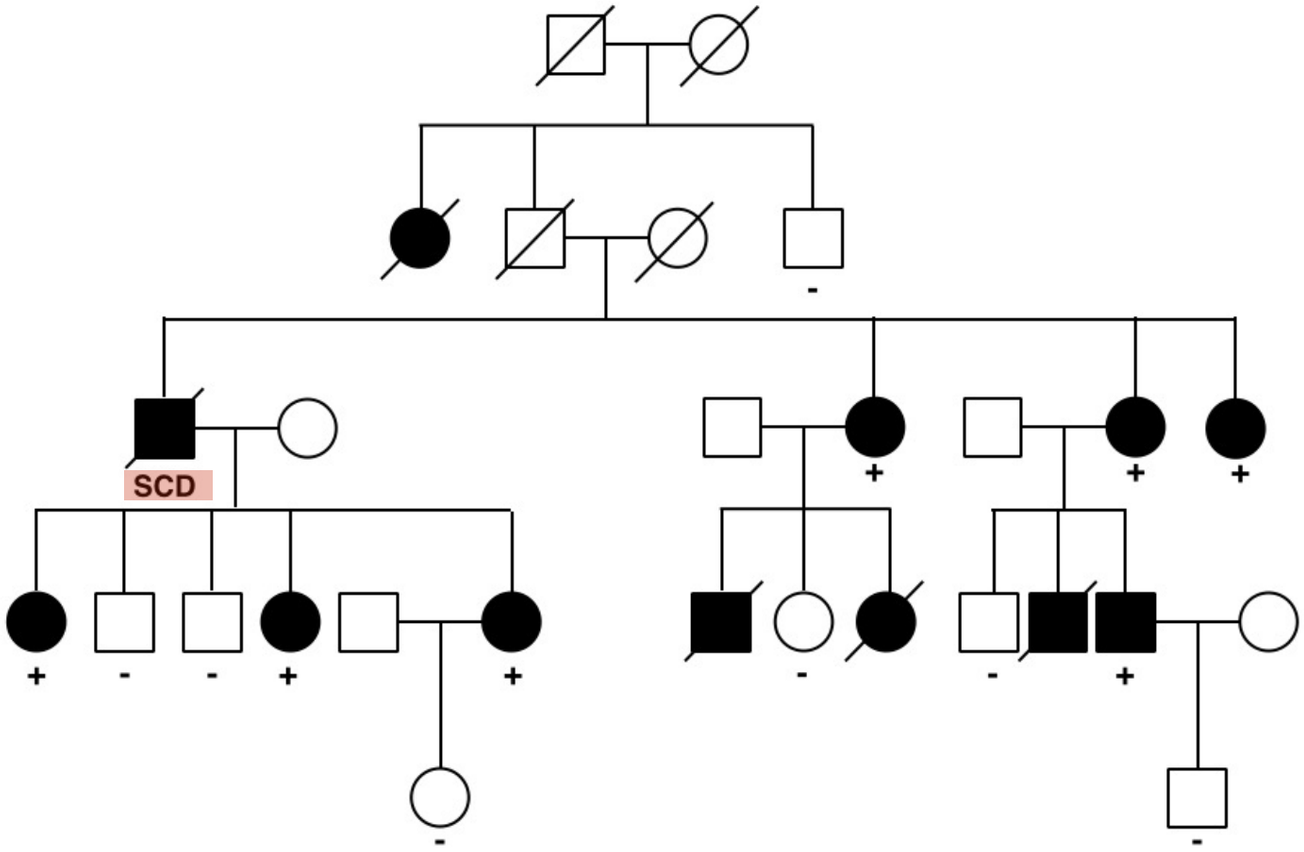
Supplementary table I. 39 Danish probands were screened for NKX2-5 mutations. Their affected relatives and accompanying malformations are shown. Three of the families are shown in pedigrees due to the size of the families (Supplementary figure I).
ASD2: secundum atrial septal defect; AVB: AV-block; AVS: aortic valve stenosis; AVSD: atrioventricular septal defect; BAV: Bicuspid aortic valve; CoA; Coarctatio of aorta; ccAVB: congenital complete AV-block; DORV: Double outlet right ventricle; d-TGA: dextro-Transposition of the great arteries; HLHS: hypoplastic left heart syndrome; MVA: Mitral valve atresia; MVS; Mitral valve stenosis; PA: Pulmonary atresia; PAPVR: Partially anomalous pulmonary venous return; PDA; Patent ductus arteriosus; PFO: Patent foramen ovale; PLSVC: Persistent left superior vena cava; PVS: Pulmonary valve stenosis;; SSS: sick sinus node syndrome; SV: single ventricle; TOF: Tetralogy of Fallot;VSDpm/musc: ventricular septal defect, perimembranous/muscular type

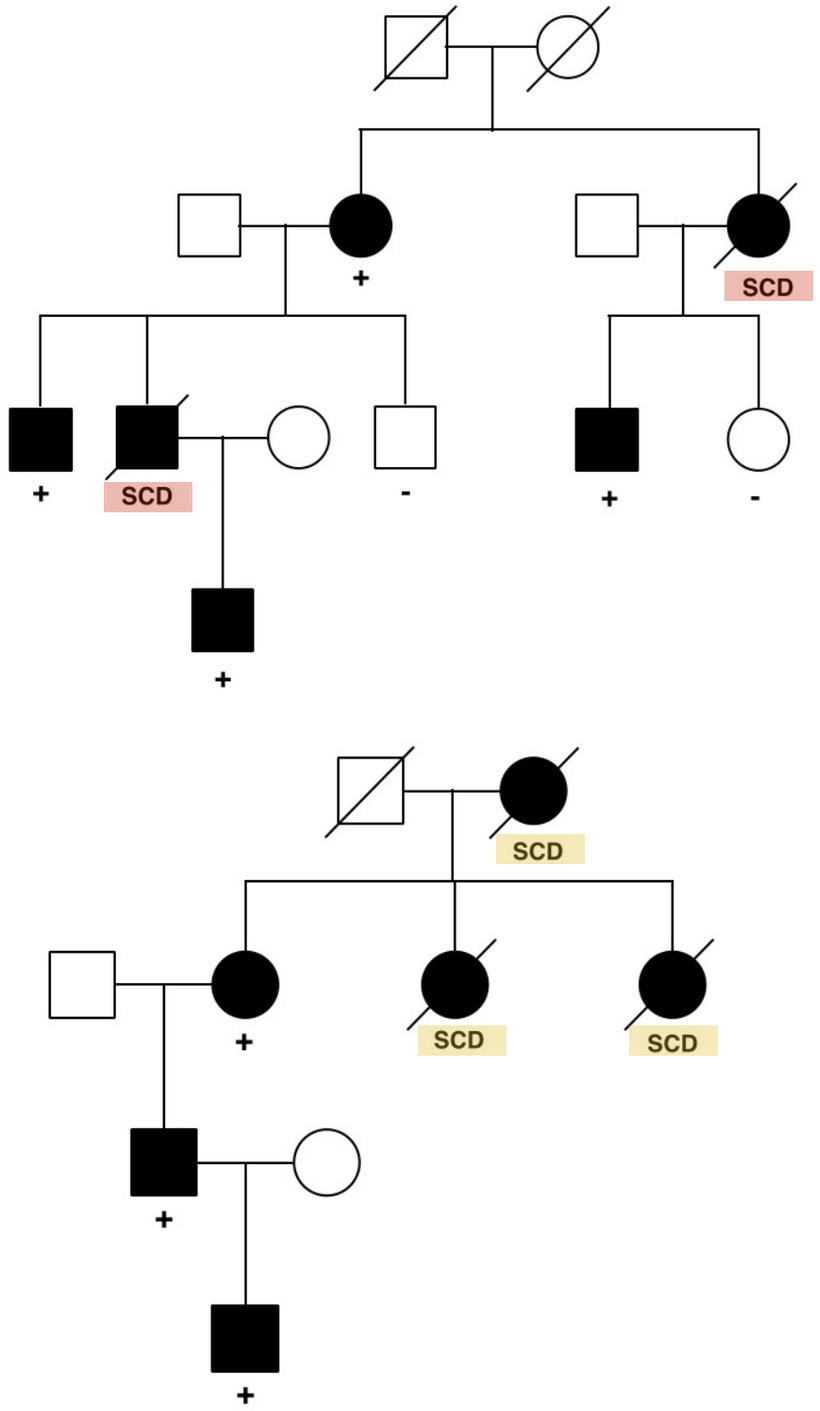
Supplementary Figure I. Pedigrees of three Danish families screened for *NKX2-5* mutations



Supplementary Figure I. Pedigrees of three Danish families, screened for *NKX2-5* mutations.
White/black = unaffected/CHD, Square/circle = Male/Female

Supplementary Figure II. Pedigrees from published papers reporting sudden cardiac deaths: Schott et al, 1999 (25)

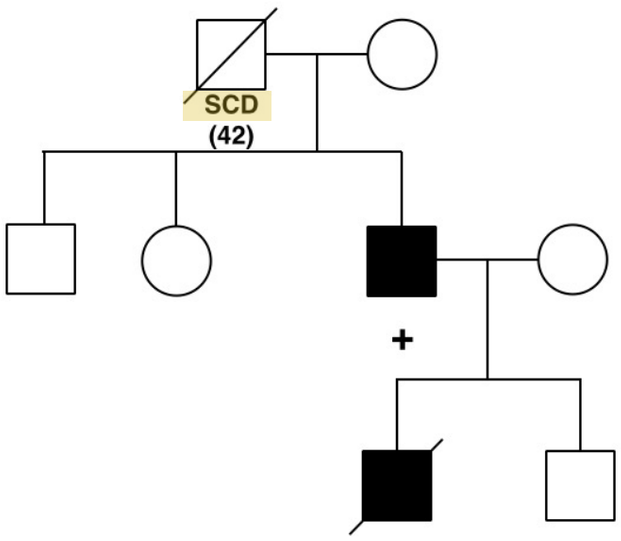




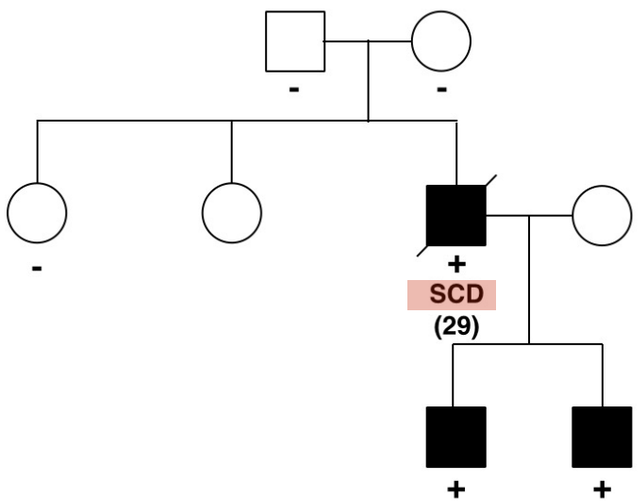
Schott JJ, Benson DW, Basson CT, et al. Congenital heart disease caused by mutations in the transcription factor NKX2-5. *Science*. 1998;281(5373):108–111

Supplementary Figure II. Schott et al reported sudden cardiac death (sudden death in otherwise healthy individual < 50 years of age) in three families. All families mainly segregated the ASD with conduction disturbance or arrhythmia. +/- = presence/absence of *NKX2-5* mutation in individual, respectively. White/black = unaffected/CHD, Square/circle = Male/Female. Red box: Obligate carriers of the mutation, yellow box: possible carriers of the mutation

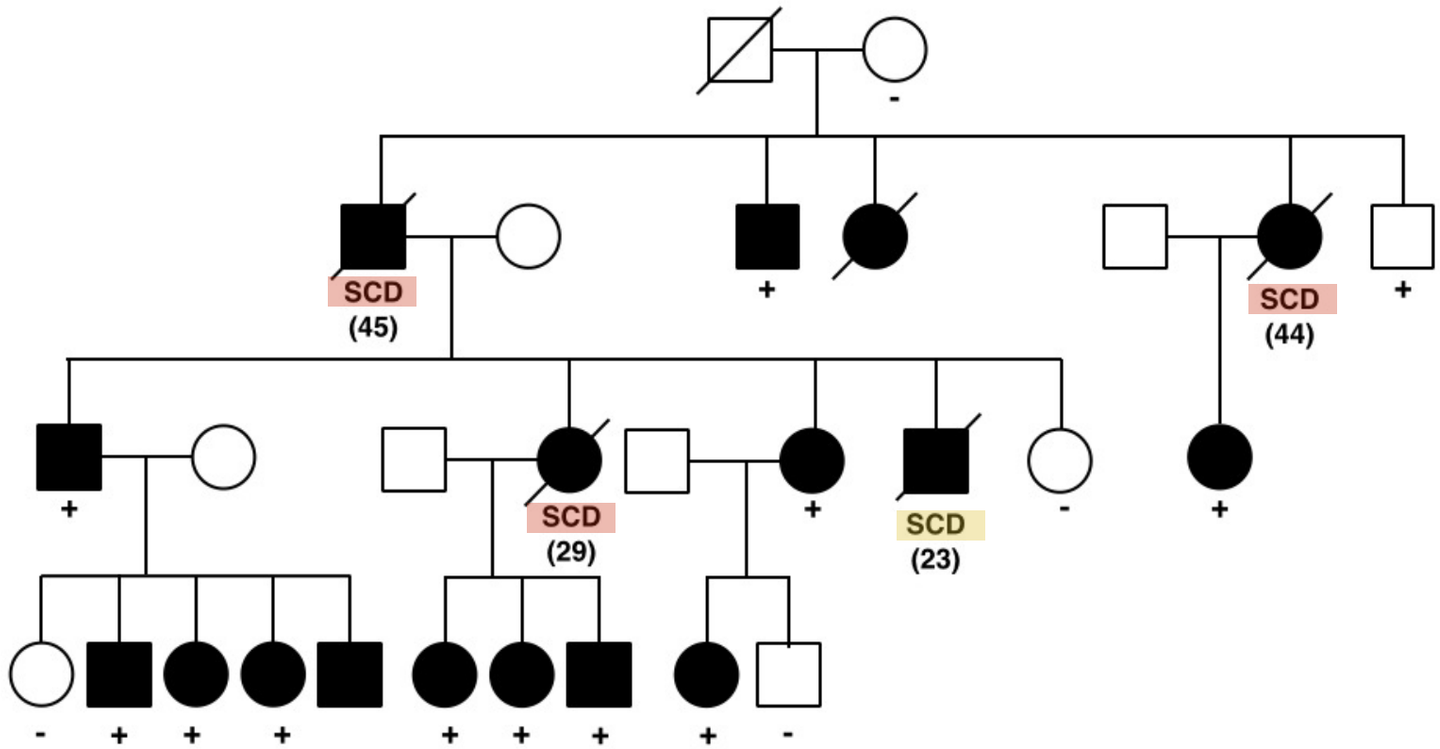
Supplementary Figure III. Pedigrees from published papers reporting sudden cardiac deaths: Hosoda et al, 1999 (50), Ouyang et al, 2011 (56) and Perera et al, 2014 (21)



Hosoda T, Komuro I, Shiojima I, et al. *Japaneese Circulation Journal*. 1999;63(5):425–6



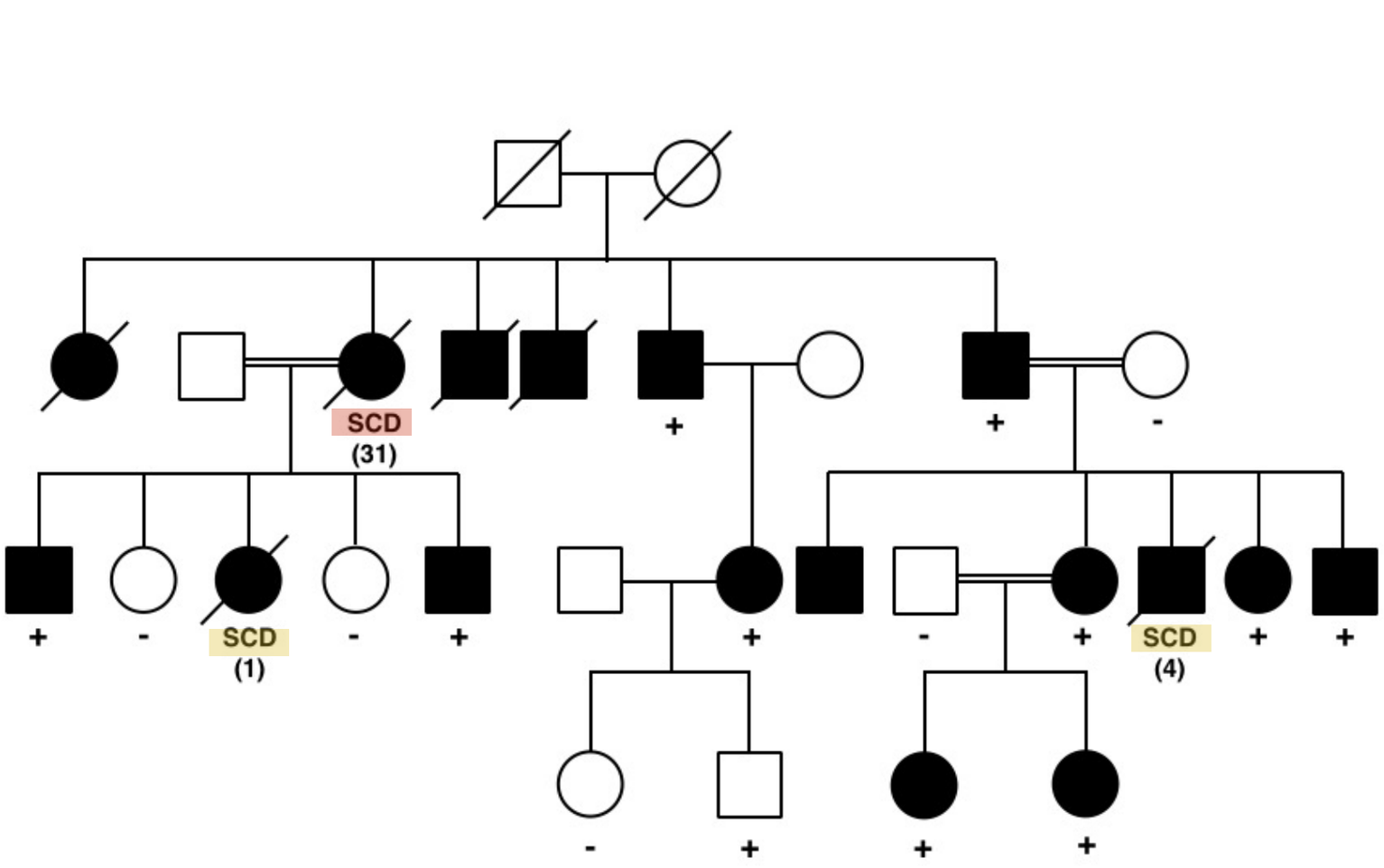
Ouyang P, Saarel E, Bai Y, et al. *Clinica Chimica Acta*. 2011;412(1-2):170–5

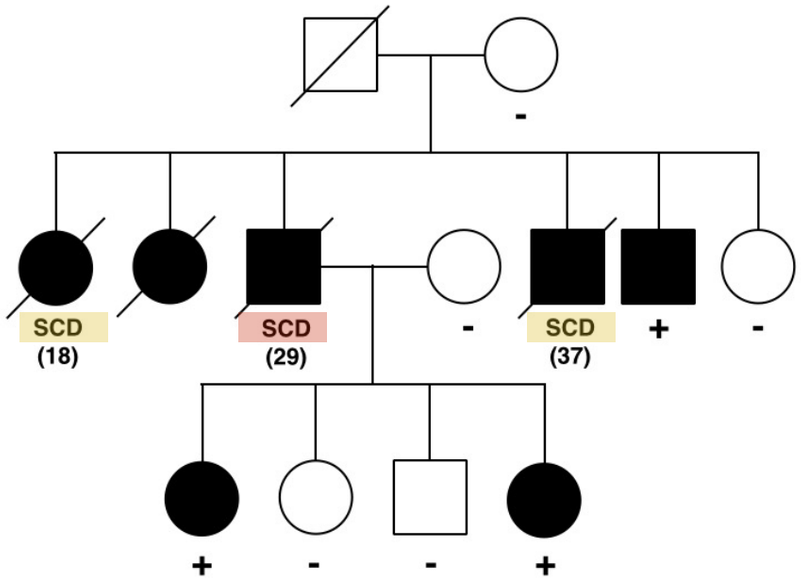


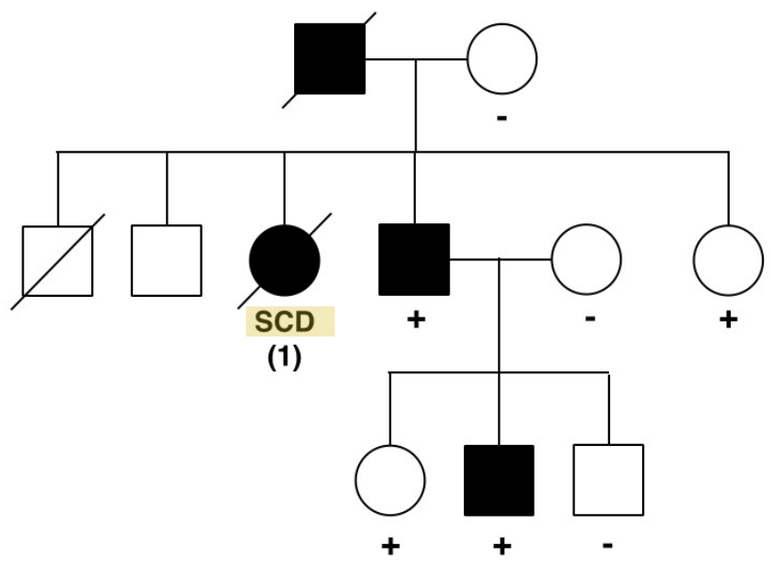
Perera JL, Johnson NM, Judge DP, Crosson JE. *Pediatric Cardiology*. 2014;35(7):1206–12

Supplementary Figure III. Sudden cardiac death (sudden death in otherwise healthy individual < 50 years of age) in three families reported by Hosoda et al, Ouyang et al and Perera et al. All families mainly segregated ASD with conduction disturbance or arrhythmia. +/- = presence/absence of *NKX2-5* mutation in individual, respectively. ()= age at sudden death if available. White/black = unaffected/CHD, Square/circle = Male/Female, Red box: obligate carrier, Yellow box: possible carrier

Supplementary Figure IV. Pedigrees from published papers reporting sudden cardiac deaths: Abou Hassan et al, 2015 (20)







Abou Hassan OK, Fahed AC, Batrawi M, et al. *Scientific Reports*. 2015;5:8848

Supplementary Figure IV. Abou Hassan et al reported sudden cardiac death (sudden death in otherwise healthy individual < 50 years of age) in three families of which one was consanguinous. All families mainly segregated ASD with conduction disturbance or arrhythmia. +/- = presence/absence of *NKX2-5* mutation in individual, respectively. ()= age at sudden death if available. White/ black = unaffected/CHD, Square/circle = Male/Female, Red box: obligate carrier, yellow box: possible carrier